

Attorney Docket No. 13054.01600

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of
Francis C. Szoka, Jr. et al.

Examiner: Schnizer

For: pH SENSITIVE LIPIDS BASED ON ORTHO
ESTER LINKERS,
COMPOSITION AND METHOD

Group Art Unit: 1635

Serial No. 09/778,388

Filed: March 7, 2001

DRAFT**DECLARATION UNDER 37 CFR 1.132**

1. I am Dr. Jorge Heller and am an expert in the field of ortho ester chemistry. I have attached a copy of my curriculum vitae as Exhibit A to this declaration.
2. I have reviewed United States Patent Application Serial No. 09/778,388 ("the '388 application") and United States Patent No. 6,200,599 ("the Nantz reference").
3. The ortho ester compositions disclosed in the '388 application share the characteristic that hydrolysis of the ortho ester bond will lead to a direct detachment of the hydrophilic portion from the hydrophobic portion of the composition. This occurs because the ortho ester attachment is through an oxygen atom.
4. The ortho ester compositions disclosed in the Nantz reference exhibit different behavior in that hydrolysis of the ortho ester functionality does not lead to a direct detachment of a hydrophilic portion from the hydrophobic portion of the composition. Instead, hydrolysis of the ortho ester first leads to intramolecular transesterification and then to detachment. This occurs because the ortho ester attachment is through a carbon atom.

5. It is my opinion that ortho esters having the characteristics disclosed in the '388 application are more typical than those disclosed in the Nantz reference. Accordingly, I believe that one of skill in the art would expect an ortho ester composition without specific indication to share the characteristics of the ortho esters of the '388 application rather than the ortho esters disclosed by the Nantz reference.
6. I acknowledge that willful false statements and the like are punishable by fine or imprisonment, or both (18 U.S.C. 1001) and may jeopardize the validity of the application or any patent issuing thereon. All statements made of my own knowledge are true and that all statements made on information and belief are believed to be true.

Date: July 10, 2003

By:

J. Heller
Dr. Jorge Heller

Jorge Heller, Ph.D. Curriculum Vitae

Dr. Jorge Heller received a B.S. degree in chemistry from the University of California in Berkeley in 1952, and a Ph.D. in physical organic chemistry from the University of Washington in Seattle in 1957.

In 1957 he joined the staff of the Union Carbide Corporation in New Jersey where he was first introduced to research in polymer science. His major emphasis at Union Carbide was mechanistic studies of Ziegler-Natta catalysis and extensions to non-hydrocarbon olefin polymerization. In 1959 he moved to the Stanford Research Institute in Menlo Park, California as a Senior Polymer Chemist where he worked on a variety of problems in synthetic polymer chemistry including work on Ziegler-Natta catalysis. In 1965 he became chairman of the Polymer Chemistry Department.

In 1970 he resigned from the Stanford Research Institute to join the Alza Corporation in Palo Alto, California as Director of Physical Sciences where he was given the responsibility of establishing a group dealing with polymer synthesis, polymer modification and polymer characterization. It was during that time that he started his research in controlled drug delivery and began his work on bioerodible polymers. The first family of poly(ortho esters), now known as Alzamer®, was synthesized during that time.

In 1974 he resigned from Alza and rejoined the staff of Stanford Research Institute, which in 1976 separated from Stanford University and changed its name to SRI International, where he became Director of the Polymer Chemistry Department and ultimately developed a group of about 30 professionals dealing with various aspects of polymer synthesis and controlled drug release. In 1980, he divided the group into two separate departments and became Director of the newly created Controlled Release and Biomedical Polymers Department. He remained in that capacity until 1990 when he gave up administrative duties for the department and became a Senior Staff Scientist.

In 1994, he left SRI International and joined Advanced Polymer Systems in Redwood City, California where he established the APS Research Institute charged with the responsibility of developing novel, APS proprietary, drug delivery technologies. He served as its Executive Director until 1997 when the APS Research Institute became part of the APS Research Department. Dr. Heller is currently Principal Scientist at APS and continues his work in controlled drug delivery with major emphasis on biodegradable polymers.

Between 1984 and 1998 Dr. Heller was Editor-in-Chief of the Journal of Controlled Release which he co-founded with Professor Feijen. He was President of the Controlled Release Society in 1989-1990 and was the Technical Program Chairman for the 10th International Symposium of the Controlled Release Society in San Francisco in 1983 and the 15th International Symposium of the Controlled Release Society in Basle, Switzerland in 1988.

Between 1970 and 1985, Dr. Heller taught a course in polymer chemistry at the San Jose State University. He currently holds appointments as Adjunct Professor at the School of Pharmacy of the University of California at San Francisco where he co-teaches a course on fundamentals of polymer science, Adjunct Professor at the University of Utah where for three years he spend July and August teaching a course in polymer synthesis, Affiliate Professor at the University of Washington, Docent at the Abo Akademii in Finland and Adjunct Professor at the Kwangju Institute of Science and Technology in Kwangju, Korea

where he teaches a biannual course in Controlled Drug Delivery. He was a Visiting Professor at the University of Geneva in 1988, a Visiting Professor at the University of Keele in England in 1989 and a Visiting Professor at the University of Utah in 1990. He is also a lecturer at the yearly MIT Controlled Release Course, now in its 20th year. Dr. Heller is the author of about 185 publications and 40 issued patents with a number pending.

Dr. Heller is, or has been, on the Scientific Advisory Board of Theratech in Salt Lake City, UT, Matrix Pharmaceuticals in Freemont, CA, Labopharm in Montreal, Canada, Hydro Med Sciences in New Brunswick, NJ, iMEDD in Columbus, Ohio, CA, and Ethical Holdings in Cambridgeshire, UK. Until recently, he was also on the Board of Directors of Advanced Polymer Systems.

Dr. Heller received a number of awards; among these are an award for best pharmaceutical paper by the Controlled Release Society in 1986, an SRI Fellowship in 1988 which provided funds for his visiting professorships, the Biomaterials Society Clemson award in Applied Biomaterials Research in 1980, an Award for Pioneering Efforts in Controlled Release presented at the Seventh International Symposium on Recent Advances in Drug Delivery held in Salt Lake City in 1995, where he was also honored, and the Controlled Release Society Distinguished Service Award in 1995. In 1993 he was elected Fellow of the American Association of Pharmaceutical Scientists, in 1994 Fellow of the Biomaterials Society and in 1996 he was admitted to the Fellowship of Biomaterials Science and Engineering.